EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	134939	sarcosine or sarcosinate or methylglycine or glycine or sarcosylate	US-PGPUB; USPAT; DERWENT	OR	ON	2007/05/22 12:08
L2	546	dimethyl adj glycine	US-PGPUB; USPAT; DERWENT	OR	ON	2007/05/22 12:08
L3	134939	l1 or l2	US-PGPUB; USPAT; DERWENT	OR	ON	2007/05/22 12:08
L4	9685	l3 and (hypohydration or rehydration or anhydration or dehydration or (loss near (water or fluid)))	US-PGPUB; USPAT; DERWENT	OR	ON	2007/05/22 12:09
L5	14091	l3 and (athel? or sport or nutrition? or diet? or dietary or drink)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/05/22 12:10
L6	1969	l4 and l5	US-PGPUB; USPAT; DERWENT	OR	ON	2007/05/22 12:10
L8	375	l6 and (choline or bursine or fagine or vidine or trimethylethanaminium or ethanaminium)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/05/22 12:13
L9	141	l6 and (betaine or lycine or oxyneurine or acidin-pepsin or betain or stea-16 or novobetaine or hepastyl or cystadane or methanamium)	US-PGPUB; USPAT; DERWENT	OR	ON	2007/05/22 12:14
L10	82	l8 and l9	US-PGPUB; USPAT; DERWENT	OR	ON	2007/05/22 12:14

National Library of Medicine - Medical Subject Headings

2007 MeSH

MeSH Supplementary Concept Data

Return to Entry Page

Name of Substance	dimethylglycine
Record Type	C
Registry Number	1118-68-9
CAS Type 1 Name	glycine, N,N-dimethyl-
Related Number	17647-86-8 (mono-K salt)
Related Number	18319-88-5 (Na salt)
Related Number	2491-06-7 (mono-HCl)
Related Number	70572-30-4 (Ca salt)
Entry Term	dimethylglycine monohydrochloride
Entry Term	dimethylglycine, calcium salt
Entry Term	dimethylglycine, monopotassium salt
Entry Term	dimethylglycine, sodium salt
Heading Mapped to	Sarcosine/*analogs & derivatives
Indexing Information	Epilepsy/drug therapy
Source	Proc Exp Biol Med 1980;164(1):9
Frequency	73
Note	metabolic product of calcium pangamate; mutagen when mixed with nitrite; RN given refers to parent cpd
Date of Entry	19800707
Revision Date	20040806
Unique ID	C025138

Return to Entry Page Link to NLM Cataloging Classification

National Library of Medicine - Medical Subject Headings

2007 MeSH

MeSH Descriptor Data

Return to Entry Page

MeSH Heading	Sarcosine
Tree Number	D12.125.481.700.374
Scope Note	An amino acid intermediate in the metabolism of choline.
Entry Term	Methylglycine
Entry Term	Magnesium Sarcosylate
Entry Term	N-Methylglycine
Entry Term	Sarcosine Hydrochloride
Entry Term	Sarcosine Monosodium Salt
Entry Term	Sodium Sarcosinate
Allowable Qualifiers	AA AD AE AG AI AN BI BL CF CH CL CS CT DE DU EC GE HI IM IP ME PD PH PK PO RE SD SE ST TO TU UR
CAS Type 1 Name	Glycine, N-methyl-
Registry Number	107-97-1
Related Number	4316-73-8 (mono-Na salt)
Related Number	637-96-7 (HCl)
Previous Indexing	Glycine (1966-1967)
Online Note	search GLYCINE 1966-67
History Note	68; was see under GLYCINE 1963-67; METHYLGLYCINE was heading 1963-95 (see under GLYCINE 1963-67)
Unique ID	D012521

MeSH Tree Structures

Amino Acids, Peptides, and Proteins [D12]
Amino Acids [D12.125]

5580856
2004/0192615
6020119
6514973
5389383

Glycine [D12.125.481]
N-substituted Glycines [D12.125.481.700]
Glycocholic Acid [D12.125.481.700.249] +
▶ Sarcosine [D12.125.481.700.374]
Thiopronine [D12.125.481.700.500]
Thiorphan [D12.125.481.700.750]

Return to Entry Page Link to NLM Cataloging Classification

National Library of Medicine - Medical Subject Headings

2007 MeSH

MeSH Descriptor Data

Return to Entry Page

MeSH Heading	Betaine
Tree Number	D02.092.877.883.077
Tree Number	D02.675.276.125
Scope Note	A naturally occurring compound that has been of interest for its role in osmoregulation. As a drug, betaine hydrochloride has been used as a source of hydrochloric acid in the treatment of hypochlorhydria. Betaine has also been used in the treatment of liver disorders, for hyperkalemia, for homocystinuria, and for gastrointestinal disturbances. (From Martindale, The Extra Pharmacopoeia, 30th ed, p1341)
Entry Term	Lycine
Entry Term	Oxyneurine
Entry Term	Acidin-Pepsin
Entry Term	Beaufour Brand of Betaine Citrate
Entry Term	Betaine Hydrochloride
Entry Term	Boizot Brand of Betaine Aspartate
Entry Term	Byk Brand of Betaine Phosphate
Entry Term	C.B.B.
Entry Term	Citrate de B챕ta챦ne Beaufour
Entry Term	Citrate de B챕ta챦ne UPSA
Entry Term	Cystadane
Entry Term	Fournier Brand of Betaine Ascorbate and Hydrate
Entry Term	Glycine Betaine
Entry Term	Hepastyl
Entry Term	Logeais Brand of Betaine Cyclobutyrate
Entry Term	Novobetaine
Entry Term	Orphan Brand of Betaine
Entry Term	Scorbo-b챕ta챦ne
Entry Term	Stea-16
Entry Term	UPSA Brand of Betaine Citrate

Allowable Qualifiers	AA AD AE AG AI AN BL CF CH CL CS CT DU EC HI IM IP ME PD PK PO RE SD ST TO TU UR
Pharm. Action	Gastrointestinal Agents
Pharm. Action	Lipotropic Agents
CAS Type 1 Name	Methanaminium, 1-carboxy-N,N,N-trimethyl-, inner salt
Registry Number	107-43-7
Related Number	590-46-5 (HCl)
History Note	68(64)
Unique ID	D001622

MeSH Tree Structures

Organic Chemicals [D02]
Amines [D02.092]
Quaternary Ammonium Compounds [D02.092.877]
Trimethyl Ammonium Compounds [D02.092.877.883]
▶ Betaine [D02.092.877.883.077]
Bethanechol Compounds [D02.092.877.883.088] +
Carnitine [D02.092.877.883.099] +
Cetrimonium Compounds [D02.092.877.883.111]
Chlorisondamine [D02.092.877.883.222]
Chlormequat [D02.092.877.883.277]
Choline [D02.092.877.883.333] +
Methacholine Compounds [D02.092.877.883.555] +
Muscarine [D02.092.877.883.777]

Organic Chemicals [D02]
Onium Compounds [D02.675]
Quaternary Ammonium Compounds [D02.675.276]

Ambenonium Chloride [D02.675.276.046]
Benzalkonium Compounds [D02.675.276.080]
Benzethonium [D02.675.276.090]
Bephenium Compounds [D02.675.276.102]
▶ Betaine [D02.675.276.125]
Betalains [D02.675.276.136] +
Bethanechol Compounds [D02.675.276.148] +
Bretylium Compounds [D02.675.276.175] +
Cetrimonium Compounds [D02.675.276.190]
Chlorisondamine [D02.675.276.200]
Chlormequat [D02.675.276.207]
(4-(m-Chlorophenylcarbamoyloxy)-2-butynyl) trimethylammonium Chloride [D02.675.276.210]
Choline [D02.675.276.232] +
Edrophonium [D02.675.276.352]
Emepronium [D02.675.276.370]
Gallamine Triethiodide [D02.675.276.400]
Glycopyrrolate [D02.675.276.425]
Hemicholinium 3 [D02.675.276.435]
Lissamine Green Dyes [D02.675.276.475]
Methacholine Compounds [D02.675.276.534] +
Bis-Trimethylammonium Compounds [D02.675.276.558] +
Muscarine [D02.675.276.580]
Neostigmine [D02.675.276.602]
Oxyphenonium [D02.675.276.648]
Propantheline [D02.675.276.700]
Tetraethylammonium Compounds [D02.675.276.787] +
Toxiferine [D02.675.276.844] +
Tubocurarine [D02.675.276.922]

Return to Entry Page Link to NLM Cataloging Classification

National Library of Medicine - Medical Subject Headings

2007 MeSH

MeSH Descriptor Data

Return to Entry Page

MeSH Heading	Choline
Tree Number	D02.033.100.291.211
Tree Number	D02.092.063.291.211
Tree Number	D02.092.877.883.333
Tree Number	D02.675.276.232
Annotation	/ biosyn / physiol permitted
Scope Note	A basic constituent of lecithin that is found in many plants and animal organs. It is important as a precursor of acetylcholine, as a methyl donor in various metabolic processes, and in lipid metabolism.
Entry Term	Bursine
Entry Term	Fagine
Entry Term	Vidine
Entry Term	2-Hydroxy-N,N,N-trimethylethanaminium
Entry Term	Choline Bitartrate
Entry Term	Choline Chloride
Entry Term	Choline Citrate
Entry Term	Choline O-Sulfate
Allowable Qualifiers	AA AD AE AG AI AN BI BL CF CH CL CS CT DU EC GE HI IM IP ME PD PH PK PO RE SD SE ST TO TU UR
Pharm. Action	Lipotropic Agents
Pharm. Action	Nootropic Agents
CAS Type 1 Name	Ethanaminium, 2-hydroxy-N,N,N-trimethyl-
Registry Number	62-49-7
Related Number	67-48-1 (Cl)
Entry Combination	deficiency:Choline Deficiency
Unique ID	D002794

MeSH Tree Structures

Organic Chemicals [D02]
- Alcohols [D02.033]
  - Amino Alcohols [D02.033.100]
    - Ethanolamines [D02.033.100.291]
      - Albuterol [D02.033.100.291.057]
      - ▶ Choline [D02.033.100.291.211]
        - Platelet Activating Factor [D02.033.100.291.211.500]
      - Clenbuterol [D02.033.100.291.231]
      - Deanol [D02.033.100.291.274]
      - Epinephrine [D02.033.100.291.310]
      - Ethanolamine [D02.033.100.291.375]
      - 2-Hydroxyphenethylamine [D02.033.100.291.410]
      - Isoproterenol [D02.033.100.291.439]
      - Labetalol [D02.033.100.291.460]
      - Midodrine [D02.033.100.291.480]
      - Norepinephrine [D02.033.100.291.502] +
      - Octopamine [D02.033.100.291.525]
      - Orciprenaline [D02.033.100.291.550] +
      - Phenylephrine [D02.033.100.291.617] +
      - Procaterol [D02.033.100.291.630]
      - Sotalol [D02.033.100.291.805]
      - Synephrine [D02.033.100.291.870]
      - Terbutaline [D02.033.100.291.905]

Organic Chemicals [D02]
- Amines [D02.092]
  - Amino Alcohols [D02.092.063]
    - Ethanolamines [D02.092.063.291]
      - Albuterol [D02.092.063.291.057]
      - ▶ Choline [D02.092.063.291.211]
        - Platelet Activating Factor [D02.092.063.291.211.500]
      - Clenbuterol [D02.092.063.291.231]
      - Deanol [D02.092.063.291.274]
      - Epinephrine [D02.092.063.291.310]
      - Ethanolamine [D02.092.063.291.375]

2-Hydroxyphenethylamine [D02.092.063.291.410]
Isoproterenol [D02.092.063.291.439]
Labetalol [D02.092.063.291.460]
Midodrine [D02.092.063.291.480]
Octopamine [D02.092.063.291.525]
Orciprenaline [D02.092.063.291.550] +
Phenylephrine [D02.092.063.291.617] +
Procaterol [D02.092.063.291.647]
Sotalol [D02.092.063.291.805]
Synephrine [D02.092.063.291.870]
Terbutaline [D02.092.063.291.905]

Organic Chemicals [D02]
Amines [D02.092]
Quaternary Ammonium Compounds [D02.092.877]
Trimethyl Ammonium Compounds [D02.092.877.883]
Betaine [D02.092.877.883.077]
Bethanechol Compounds [D02.092.877.883.088] +
Carnitine [D02.092.877.883.099] +
Cetrimonium Compounds [D02.092.877.883.111]
Chlorisondamine [D02.092.877.883.222]
Chlormequat [D02.092.877.883.277]
▶ Choline [D02.092.877.883.333]
Benzoylcholine [D02.092.877.883.333.100]
Carbachol [D02.092.877.883.333.115]
Cytidine Diphosphate Choline [D02.092.877.883.333.130]
Phosphorylcholine [D02.092.877.883.333.700]
Platelet Activating Factor [D02.092.877.883.333.710]
Propylbenzilylcholine Mustard [D02.092.877.883.333.720]
Succinylcholine [D02.092.877.883.333.780]
Thiocholine [D02.092.877.883.333.800] +
Methacholine Compounds [D02.092.877.883.555] +
Muscarine [D02.092.877.883.777]

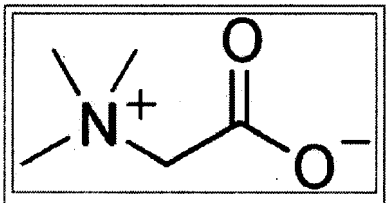
Organic Chemicals [D02]
Onium Compounds [D02.675]

Quaternary Ammonium Compounds [D02.675.276]
- Ambenonium Chloride [D02.675.276.046]
- Benzalkonium Compounds [D02.675.276.080]
- Benzethonium [D02.675.276.090]
- Bephenium Compounds [D02.675.276.102]
- Betaine [D02.675.276.125]
- Betalains [D02.675.276.136] +
- Bethanechol Compounds [D02.675.276.148] +
- Bretylium Compounds [D02.675.276.175] +
- Cetrimonium Compounds [D02.675.276.190]
- Chlorisondamine [D02.675.276.200]
- Chlormequat [D02.675.276.207]
- (4-(m-Chlorophenylcarbamoyloxy)-2-butynyl) trimethylammonium Chloride [D02.675.276.210]
- ▶ Choline [D02.675.276.232]
  - Benzoylcholine [D02.675.276.232.100]
  - Carbachol [D02.675.276.232.115]
  - Cytidine Diphosphate Choline [D02.675.276.232.130]
  - Phosphorylcholine [D02.675.276.232.700]
  - Platelet Activating Factor [D02.675.276.232.710]
  - Propylbenzilylcholine Mustard [D02.675.276.232.720]
  - Succinylcholine [D02.675.276.232.780]
  - Thiocholine [D02.675.276.232.800] +
- Edrophonium [D02.675.276.352]
- Emepronium [D02.675.276.370]
- Gallamine Triethiodide [D02.675.276.400]
- Glycopyrrolate [D02.675.276.425]
- Hemicholinium 3 [D02.675.276.435]
- Lissamine Green Dyes [D02.675.276.475]
- Methacholine Compounds [D02.675.276.534] +
- Bis-Trimethylammonium Compounds [D02.675.276.558] +
- Muscarine [D02.675.276.580]
- Neostigmine [D02.675.276.602]
- Oxyphenonium [D02.675.276.648]
- Propantheline [D02.675.276.700]
- Tetraethylammonium Compounds [D02.675.276.787] +
- Toxiferine [D02.675.276.844] +
- Tubocurarine [D02.675.276.922]

Return to Entry Page Link to NLM Cataloging Classification

Trimethylglycine

From Wikipedia, the free encyclopedia



Trimethylglycine

Trimethylglycine (also commonly known as **TMG, betaine, glycine betaine** or **betaine anhydrous**) is more specifically **N,N,N-trimethylglycine**. Trimethylglycine was originally named betaine after its discovery in sugar beets (*Beta vulgaris*) in the 19th century. It is a small N-trimethylated amino acid, existing in zwitterionic form at neutral pH. This substance is often called "glycine betaine" to distinguish it from other betaines that are widely distributed in microorganisms, plants and animals. TMG is not to be confused with betaine hydrochloride.

Trimethylglycine is an organic compound with a structure similar to **choline** and a betaine. The molecular structure is $(CH_3)_3NCH_2COOH$ as a cation with either the carboxylic acid as the anion (loss of proton) or another anion present. The difference is that **choline** (trimethylaminoethanol) has been reduced from a terminal carboxylic acid to a hydroxyl group. If Trimethylglycine donates one of its **methyl** groups, then it becomes dimethylglycine.

Alkylated derivates of trimethylglycine have use as quaternary ammonium zwitterionic surfactants.

Contents

Sources

Betaine is obtained by humans from foods, either as betaine or **choline**-containing compounds. Food

items with the highest content of betaine are wheat, spinach, shellfish and sugar beets. Estimates of betaine intake are from 0.1 to 1 g/day and as high as 2.5 g/day for a diet high in whole wheat and seafood. Thus, the intake depends on food composition, but is probably also related to production of the food items, including growing and osmotic conditions. Alternatively, betaine is formed from **choline**.

The conversion of **choline** to betaine is a two-step enzymic process, which takes place in the liver and kidney. **Choline** is first oxidised to betaine aldehyde, a reaction catalysed by the mitochondrial **choline** oxidase (**choline** dehydrogenase, EC 1.1.99.1), and betaine aldehyde is further oxidised in the mitochondria or cytoplasm to betaine by betaine aldehyde dehydrogenase (EC 1.1.1.8).

Functions

Betaine has three known functions in mammals. It is an organic osmolyte that accumulates in renal medullary cells and some other tissues to balance extracellular hypertonicity. Secondly, it also acts like a chaperone to stabilise protein structure under denaturing conditions. Finally, it serves as a **methyl donor** in the betaine homocysteine methyltransferase (BHMT) reaction which converts homocysteine to methionine.

Therapeutic uses

Trimethylglycine is used to treat high homocysteine levels.[1] Kilmer S. McCully, MD, theorised that cholesterol and clogged arteries were symptoms rather than causes of heart disease and proposed homocysteine as a more likely culprit. If it were not for his work, homocysteine would not have been thought harmful and so supplements to lower homocysteine would not have been thought necessary.

TMG may also have uses in enhancing mood, as **methyl donor** it helps increase SAMe levels.

A compound which may be confused with TMG is betaine hydrochloride, or betaine HCl. Betaine HCl is used as a digestive aid; it is particularly helpful for persons with insufficient acid production in the stomach. Betaine HCl has an acidic taste. TMG (anhydrous betaine) tastes sweet with a metallic aftertaste and is usually produced from sugar beets.

After giving off a **methyl** group TMG becomes dimethylglycine. DMG helps increase oxygenation to cells and athletes have used it to increase performance. TMG is used by the ton in livestock farming, paired with lysine to increase "carcass yield," to help increase muscle mass. It is also used in salmon farming to relieve osmotic pressure in cells as the animals make the switch from saltwater to freshwater.

Laboratory studies have shown promise for TMG in the treatment of nonalcoholic steatohepatitis. [2]

Biochemical mechanisms

TMG functions very closely with **choline**, folic acid, vitamin B12 and S-adenosyl methionine SAMe. All of these compounds function as "**methyl** donors." They carry and donate **methyl** functional groups to facilitate necessary chemical processes. The donation of **methyl** groups is important to proper liver function, cellular replication, and detoxification reactions. TMG also plays a role in the manufacture of carnitine and serves to protect the kidneys from damage.

Methyl donors, DNA and cancer - DNA methylation is central to the establishment and heritability of states of expression. Gene silencing that is dependent on DNA methylation involves histone deacetylation. The relevance of the correct maintenance of these modification patterns is illustrated by cancer, in which alterations in DNA methylation occur. Hypomethylation is associated with chromosomal instability. [3] Methionine is formed from Homocysteine and is converted to SAMe, the human body's predominant **methyl donor**. In 1985, studies were conducted into Methionine metabolism and cancer. One paper summarised the most recent developments linking methionine metabolism and SAMe to DNA methylation and gene expression in relation to cancer. The study stated that "recent evidence suggests that enzymatic DNA methylation is an important component of gene control and may serve as a silencing mechanism for gene function. Some carcinogens interfere with enzymatic DNA methylation, and thus may allow oncogene activation". The author (J van der Westhuyzen) also wrote that demethylation may be a necessary condition for enhanced transcription and pointed out that DNA hypomethylation has been observed in many cancer cells and tumours. [4] In 2002 LL Wu and JT Wu of the University of Utah Health Science Centre published a study [5] making the claim that circulating total Homocysteine "may be used as a more accurate tumour marker for monitoring cancer patients during treatment, and hyperhomocysteinemia [may be used] as a risk factor for carcinogenesis". Trimethylglycine / betaine donates a **methyl** group to convert homocysteine to methionine (using Vitamin B6 and Zinc as co-factors) in a reaction catalysed by BHMT (the Betaine-Homocysteine-**Methyl**-Transferase enzyme). Methionine is then converted to SAMe by Methionine Adenosyl Transferase (MAT) using Magnesium and Adenosine Triphosphate as co-factors.

Trimethylglycine in Molecular Biology

Trimethylglycine is an adjuvant of the Polymerase Chain Reaction (PCR) and of all DNA polymerisation based assays such as DNA sequencing. By an unknown Function it aids in the prevention of secondary structures in the DNA molecules and prevents the problems associated with the amplification and sequencing of GC rich regions. Trimethylglycine makes Guanosine and Cytidine (Strong binders) behave with thermodynamics similar to those of Thymidine and Adenosine (Weak Binders). It is best used at a final concentration of 1M.

References

1. ^ Holm PI, Ueland PM, Vollset SE, Midttun O, Blom HJ, Keijzer MB, den Heijer M. (2005) *Betaine and folate status as cooperative determinants of plasma homocysteine in humans.* Arterioscler Thromb Vasc Biol. 379-85. PMID 15550695 (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15550695)
2. ^ Angulo P, Lindor KD (2001). "Treatment of nonalcoholic fatty liver: present and emerging therapies". *Semin Liver Dis* **21** (1): 81-88. DOI:10.1055/s-2001-12931 (http://dx.doi.org/10.1055/s-2001-12931).
3. ^ doi: 10.1038/npg.els.006158
4. ^ Nutr Cancer 1985; 7(3):179-83
5. ^ Clin Chim Acta 2002 Aug;322(1-2):21-8

External links

- USDA Database for the **Choline** Content of Common Foods (http://www.nal.usda.gov/fnic/foodcomp/Data/Choline/Choline.html) - including the data on **choline** metabolites, such as betaine, in 434 food items.

- Links to external chemical sources

Retrieved from "http://en.wikipedia.org/wiki/Trimethylglycine"

Categories: Biochemistry | Quaternary ammonium compounds

A FURTHER INVESTIGATION OF THE ABILITY OF SARCOSINE TO SERVE AS A LABILE METHYL DONOR*

By VINCENT DU VIGNEAUD, SOFIA SIMMONDS, AND MILDRED COHN

(From the Department of Biochemistry, Cornell University Medical College, New York City)

(Received for publication, August 3, 1946)

It is the purpose of the present paper to report a study of transmethylation with isotopic sarcosine. The sarcosine used in these experiments was labeled with deuterium in the methyl group and also with N^{15}. The compound was fed to four adult rats for 7 days as a supplement to an otherwise methyl-free diet containing homocystine. At the end of this time, the rats were sacrificed and choline, creatine, glycine, and glutamic acid were isolated from the tissues of each rat. In order to determine the relative efficacy of sarcosine as a methyl donor, a parallel experiment under identical conditions was carried out with isotopic choline. In the latter compound, only the methyl groups were labeled. The data from these experiments are summarized in Table I.

As shown in Table I, sarcosine was not an effective methyl donor for the synthesis of choline and creatine, although a small fraction of the methyl groups of these tissue constituents was derived from the dietary sarcosine. About 1 to 2 per cent of the methyl groups of choline and about 0.5 per cent of the methyl group of creatine were derived from the sarcosine in 7 days. When an amount of methyl groups equivalent to that supplied as isotopic sarcosine was fed in the form of deuteriocholine, approximately 22 per cent of the tissue choline-methyl and approximately 2 per cent of the creatine-methyl groups were derived from the diet.

In order to eliminate variations due to differences in body weight of the rats and differences in amounts of test compound ingested, the data may be recalculated on the basis of mM of test compound ingested per 100 gm. of body weight. When the data are recalculated in this manner (Table II), the creatine N^{15} values resulting from the feeding of isotopic sarcosine appear to exhibit a random fluctuation within ± 10 per cent. On the other hand, the variation of deuteriomethyl concentration in the creatine is of a different order of magnitude; approximately 70 per cent more methyl groups of creatine have been derived from dietary sarcosine in the female rats than in the male rats. A similar recalculation of the data from the feeding of choline (Table II) shows no significant difference between the

* The authors wish to thank the Nutrition Foundation, Inc., for the research grant which has aided this work.

TABLE I

Feeding Experiments with Isotopic Sarcosine Hydrochloride (88.9 Atom Per Cent D in Methyl Group, 4.17 Atom Per Cent Excess N^{15}) and with Deuteriocholine Chloride (83.1 Atom Per Cent D in Methyl Groups) for 7 Days

Rat No. and sex	Compound fed	Change in body weight	Per cent of methyl or N in isolated compounds derived from test compounds						
			Choline		Creatine			Glycine	Glutamic acid
			Total methyl	Nitrogen	Methyl	Total nitrogen	Sarcosine nitrogen*	Nitrogen	Nitrogen
		gm.							
1752 ♂	N^{15} deuteriosarcosine hydrochloride	364–330	1.11 ± 0.08	1.39 ± 0.07	0.29 ± 0.10	1.03 ± 0.07	2.5	1.94 ± 0.07	0.50 ± 0.07
1753 ♂		350–310	1.39 ± 0.08	1.51 ± 0.07	0.43 ± 0.10	1.03 ± 0.07	2.5	2.44 ± 0.07	0.48 ± 0.07
1755 ♀		328–293	1.46 ± 0.04	1.53 ± 0.07	0.63 ± 0.10	1.25 ± 0.07	3.0	2.66 ± 0.07	0.53 ± 0.07
1757 ♀		278–259	2.16 ± 0.08	1.92 ± 0.07	0.82 ± 0.10	1.41 ± 0.07	3.4	2.88 ± 0.07	0.65 ± 0.07
1754 ♂	Deuteriocholine chloride	355–344	21.3 ± 0.18		2.07 ± 0.24				
1760 ♀		296–288	22.6 ± 0.18		2.12 ± 0.24				

* N^{15} of sarcosine moiety of creatine calculated on basis of N^{15} distribution data of Bloch and Schoenheimer (1).

male and the female rat. The sarcosine results with respect to sex difference will bear further experimental investigation.

A comparison of the percentage of methyl groups[1] and nitrogen in the isolated choline derived from the fed sarcosine shows that the sarcosine molecule is not converted to choline as a whole. Of even greater interest is a similar comparison in the isolated creatine which reveals that the sarcosine molecule is not converted intact to creatine but first is demethylated to yield glycine. This is in agreement with the experimental findings of Bloch and Schoenheimer (1, 2) and of Borsook and Dubnoff (3).

TABLE II

Data from Table I Recalculated on Basis of mM of Test Compound Ingested Per 100 Gm. of Body Weight

Rat No. and sex	mM test compound ingested in 7 days per 100 gm. body weight	Per cent of methyl or N in isolated compounds derived from test compounds					
		Choline		Sarcosine moiety of creatine		Glycine	Glutamic acid
		Total methyl	Nitrogen	Methyl	Nitrogen	Nitrogen	Nitrogen
N^{15} deuteriosarcosine hydrochloride							
1752 ♂	2.29	0.485	0.606	0.127	1.08	0.846	0.218
1753 ♂	2.56	0.543	0.590	0.168	0.97	0.953	0.188
1755 ♀	2.56	0.570	0.597	0.246	1.17	1.04	0.207
1757 ♀	3.14	0.688	0.611	0.261	1.08	0.918	0.207
Deuteriocholine chloride							
1754 ♂	2.45*	8.70		0.845			
1756 ♀	2.93*	7.71		0.724			

* This figure represents the number of milliequivalents of methyl groups rather than of choline.

With the data available from the present study with sarcosine, it is now possible to compare the three N-methylglycine derivatives, sarcosine, dimethylglycine, and betaine, as methyl donors. Although a direct comparison among these compounds cannot be made because the sarcosine was fed to adult rats, whereas the dimethylglycine and betaine were fed to growing rats (4), the relative activity of each compound can be evaluated nevertheless by comparison with choline fed under the same conditions. Such a

[1] The figures in Tables I and II represent the percentage of three methyl groups of choline derived from sarcosine. If one considered only one methyl group of choline which would be necessary for a direct conversion of sarcosine to choline, the value would be three times as high.

comparison shows that betaine (4) is by far the most active of the three glycine derivatives. Dimethylglycine (4) and sarcosine are both relatively inactive. This is in agreement with the fact that betaine is the only one which can replace choline in the growth tests (5, 6).

EXPERIMENTAL

Synthesis of N^{15} Deuteriosarcosine Hydrochloride ($CD_3N^{15}HCH_2COOH \cdot HCl$)—Isotopic sarcosine hydrochloride was prepared from N^{15} glycine (4) and deuteriomethyl iodide (7) by the method of Fischer and Bergmann (8).

Analysis—

N^{15} deuteriosarcosine hydrochloride.	Calculated.[2]	N 10.92
	Found.	" 10.53

The compound contained 82.9 atom per cent excess deuterium in the methyl group and 4.17 atom per cent excess N^{15}.

Feeding of N^{15} Deuteriosarcosine—Four adult rats, two males and two females, ranging in weight from 280 to 360 gm., were used. The isotopic sarcosine hydrochloride, with sufficient $NaHCO_3$ to neutralize it, was incorporated in a diet containing 1.25 per cent homocystine (4) and was the only possible source of labile methyl groups in the diet. For the first 4 days of the feeding period, 2.2 gm. of isotopic sarcosine hydrochloride were added per 100 gm. of diet. Since the daily food intake was somewhat lower than expected, it was necessary to give additional isotopic sarcosine hydrochloride, neutralized with $NaHCO_3$, in the aqueous solution of B vitamins (4) in order to maintain the total intake of sarcosine hydrochloride at approximately 150 mg. per rat daily.

To avoid giving the sarcosine in both the diet and the B vitamin supplement, during the last 3 days of the experiment 3.2 gm. of the isotopic sarcosine hydrochloride were added per 100 gm. of diet. During the entire 7 day feeding period, each rat ingested a total of approximately 1.03 gm. of test compound, which corresponds to a daily intake of sarcosine equivalent in methyl groups to 58 mg. of choline chloride.

At the end of the 7 day experimental feeding period, choline was isolated as the chloroplatinate and creatinine as creatinine potassium picrate from the tissues of the sacrificed animals (7); for the N^{15} analyses, picric acid was removed from creatinine potassium picrate (4). Glycine and glutamic acid also were isolated from the tissue proteins. Glycine was isolated as the trioxalatochromiate, which was converted, for the purpose of analyses, to carbobenzoxyglycine (4, 9). Glutamic acid was isolated as glutamic acid hydrochloride (4, 10). The pertinent data from this experiment are summarized in Table I.

[2] All calculated values are based on increased molecular weights due to deuterium in the molecule.

Analyses—Choline chloroplatinate

Rat 1752.	Calculated,[3]	Pt 31.7;	found,	Pt 31.4
" 1753.	"	" 31.7;	"	" 31.5
" 1755.	"	" 31.6;	"	" 31.7
" 1757.	"	" 31.6;	"	" 31.2

Carbobenzoxyglycine

Rat 1752.	Calculated,	N 6.70;	found,	N 6.41
" 1753.	"	" 6.70;	"	" 6.58
" 1755.	"	" 6.70;	"	" 6.62
" 1757.	"	" 6.70;	"	" 6.58

Glutamic acid hydrochloride

Rat 1752.	Calculated,	N 7.63;	found,	N 7.41
" 1753.	"	" 7.63;	"	" 7.64
" 1755.	"	" 7.63;	"	" 7.46
" 1757.	"	" 7.63;	"	" 7.67

Feeding of Deuteriocholine Chloride ($(CD_3)_3N(Cl)CH_2CH_2OH$)—Two adult rats, one male and one female weighing 355 and 296 gm. respectively, were maintained on the same homocystine diet (4) as used in the preceding experiment. 29 mg. of deuteriocholine chloride (7) in the aqueous solution of B vitamins (4) were fed twice daily to each rat. The deuteriocholine chloride (7) contained 83.1 atom per cent excess deuterium in the methyl groups. After 7 days, the rats were sacrificed and tissue choline and creatine were isolated (7). The data from this experiment are summarized in Table I.

Analyses—Choline chloroplatinate

Rat 1754.	Calculated,[3]	Pt 31.5;	found,	Pt 31.2
" 1756.	"	" 31.5;	"	" 31.7

SUMMARY

The ability of sarcosine to serve as a methyl donor for creatine and choline has been investigated by feeding adult rats N^{15} deuteriosarcosine ($CD_3N^{15}HCH_2COOH$). Transmethylation from dietary sarcosine to tissue choline and creatine was observed, but the apparent rate of these reactions was slow, as compared to the rate at which methyl groups of dietary deuteriocholine appear in the choline and creatine of the tissues.

The authors wish to thank Dr. D. Rittenberg and Mr. I. Sucher of the Department of Biochemistry, College of Physicians and Surgeons, Columbia University, for the N^{15} analyses, and Mr. R. C. Funk, Jr., for the elementary analyses reported in this paper.

BIBLIOGRAPHY

1. Bloch, K., and Schoenheimer, R., *J. Biol. Chem.*, **138**, 167 (1941).
2. Bloch, K., and Schoenheimer, R., *J. Biol. Chem.*, **135**, 99 (1940).
3. Borsook, H., and Dubnoff, J. W., *J. Biol. Chem.*, **138**, 389 (1941).

4. du Vigneaud, V., Simmonds, S., Chandler, J. P., and Cohn, M., *J. Biol. Chem.*, **165**, 639 (1946).
5. du Vigneaud, V., Chandler, J. P., Moyer, A. W., and Keppel, D. M., *J. Biol. Chem.*, **131**, 57 (1939).
6. Moyer, A. W., and du Vigneaud, V., *J. Biol. Chem.*, **143**, 373 (1942).
7. du Vigneaud, V., Cohn, M., Chandler, J. P., Schenck, J. R., and Simmonds, S., *J. Biol. Chem.*, **140**, 625 (1941).
8. Fischer, E., and Bergmann, M., *Ann. Chem.*, **398**, 96 (1913).
9. Bergmann, M., and Niemann, C., *J. Biol. Chem.*, **122**, 577 (1937–38).
10. Stetten, D., Jr., *J. Biol. Chem.*, **140**, 143 (1940).

Day : Tuesday
Date: 5/22/2007

Time: 12:20:41

PALM INTRANET

Inventor Information for 10/697428

Inventor Name	City	State/Country
VERLAAN, GEORGE	WAGENINGEN	NETHERLANDS
HAGEMAN, ROBERT JOHAN JOSEPH	WADDINXVEEN	NETHERLANDS
LODEWIJK SMEETS, RUDOLF LEONARDUS	VENLO	NETHERLANDS

Appln Info | Contents | Petition Info | Atty/Agent Info | Continuity/Reexam | Foreign D

Search Another: Application# [ ] Search **or Patent#** [ ] Search

PCT / [ ] / [ ] Search **or PG PUBS #** [ ] Search

Attorney Docket # [ ] Search

Bar Code # [ ] Search

To go back use Back button on your browser toolbar.

Back to PALM | ASSIGNMENT | OASIS | Home page